CURRICULUM VITAE

Name:	DAVID M. ORNITZ, M.D., Ph.D.	
Home address:	11206 Mosley Farm Court	(314) 569-4223
	Creve Coeur, MO 63141	
Work address:	Department of Molecular Biology and Pharmacology	(314) 362-3908 office
	Washington University Medical School, Box 8103	(314) 362-5074 lab
	660 South Euclid Avenue	(314) 362-7058 FAX
	St. Louis, MO 63110	dornitz@wustl.edu
Date of birth:	June 3, 1959	
Place of birth:	New Haven, CT, USA	

Education

B.S. degree, Biochemistry, University of California, Davis, June 1981
Ph.D. degree, Biochemistry, University of Washington, March 1987
M.D. degree, University of Washington, June 1988
Postdoctoral Fellow, Genetics, Harvard Medical School, July 1988-April 1992

Scholarships and Awards

American Heart Association Established Investigator Award
Arnold and Mabel Beckman Young Investigators Award
Lucille Markey Award
Medical Scientist Training Program
American Heart Association Student Research Associates Program

Positions Held

10/1/04-present Interim Head, Department of Molecular Biology and Pharmacology

4/02-present Alumni Endowed Professor of Molecular Biology and Pharmacology

7/00-present Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.

11/96-6/00. Associate Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.

5/92-10/96. Assistant Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.

7/88-4/92. Postdoctoral Fellow with Dr. Philip Leder, Department of Genetics, Harvard Medical School. Development of a yeast GAL4/UAS binary genetic system to regulate transgene expression in mice. Expression of the *int2* gene in the mammary gland and prostate of transgenic mice. Biochemical analysis of FGF2/FGF receptor binding interactions. Cloning of a novel FGF receptor. Deregulated expression of Leukemia inhibitory factor in T-cells of transgenic mice. Transactivation of HTLV-I LTR-*myc* fusion genes by the HTLV-I-*tax* gene in transgenic mice.

7/83-3/87. Ph.D. thesis research with Dr. Richard Palmiter, Department of Biochemistry, University of Washington. Regulation of tissue-specific gene expression in the pancreas and liver of transgenic mice. Targeted oncogenesis of the mouse pancreas with SV40 T antigen and H-*ras*.

1/80-6/81. Undergraduate research with Dr. Irwin H. Segel, Department of Biochemistry, University of California, Davis. The kinetic mechanism of the enzyme Nitrate Reductase.

1/79-12/79. Undergraduate research with Dr. Don Bergstrom, Department of Chemistry, University of California, Davis. Synthetic organic chemistry of nucleosides.

1/77-8/79. American Heart Association Student Research Associates Program with Dr. George Popjak, Department of Biological Chemistry, University of California, Los Angeles. Enzymology of cholesterol biosynthesis.

Patents

Yayon, A., Ornitz, D.M., Klagsbrun, M., Leder, P. (1993) Cells expressing a substantial number of surface high affinity HBGF receptors but relatively few low affinity HBGF binding sites and a system for assaying binding to HBGF receptor. US Patent No. 5,270,197. Harvard Medical School

Ornitz, D.M. (1998) Method for identifying molecules that regulate FGF activity. U.S. Patent No. 5,733,893 and No. 5,891,655 (divisional). Monsanto-Searle Inc.

Ward, B., Ornitz, D.M., Deines, M., Bittick, T. (pending) Tracer reagents that enhance reaction-product analysis.-Sigma Chemical Co.

Ornitz, D.M. and Colvin, J.C. (2000) Animal model with disrupted *Fgf9* gene. Monsanto-Searle Inc., Patent No. 6,136,040.

Independent Funding

Past

SBIR grant with Reliable Biopharmaceuticals, 1994, Regulators of fibroblast growth factor activity, $16,666 total costs

Arnold and Mabel Beckman Young Investigators Award, 7/1/94-6/30/96, $100,000/year direct costs

Monsanto/Searle research award. 1/1/94-12/31/96, $64,000/year

Monsanto/Searle research award. 1/1/97-12/31/99, $70,000/year

Pharmacia/Monsanto research award. 6/1/01-12/31/01, $37,000

ZymoGenetics Inc. 11/99-10/00, $53,260 direct . *Fgf18* function in mouse development.

American Heart Association established investigator award, Regulation of cardiac and aortic arch development by fibroblast growth factors 9 and 11, 1/1/98-12/31/01, $75,000/year direct costs

NIH grant R01 CA60673, The role of FGF receptors in cell growth and neoplasia. 4/1/94-3/30/99; $110,387/year direct costs, Renewed as "FGFs involved in cerebellar development". 4/1/99-1/31/04; $153,498/year direct costs.

NIH grant R01 DC04289, (PI: Yi Rao) Molecular guidance of neuronal migration. (co-PI, DMO), 8/1/00-7/31/03.

NIH grant R01 HD35692, FGF signaling in bone growth and development, 7/1/97-6/30/01, Renewed as P01 HD39952, start date 4/1/01-3/31/06, Mechanisms of Growth and Overgrowth Syndromes, $194,168/year direct costs.

Pfizer grant, Modulation of cardiac hypertrophy by FGF signaling. 1/01/04-12/31/05, $100,000/year direct costs

March of Dimes, Regulation of Lung Development by Fibroblast Growth Factor 9. 6/1/02-5/31/05, $74,142/year direct costs.

Current

NIH grant RO1 DC02236, Genes involved in the development of vestibular otoconia, 1/1/95-12/31/98, Renewed, 7/1/99-6/31/04, 7/21/04-6/30/07

March of Dimes, Signaling pathways regulating lung mesenchyme development. 6/1/06-5/31/09

NIH R01 HL076664-04, FGF regulation of cardiac development and function, 12/01/04-11/30/08.

NIH R01 HD049808, FGFs in skeletal development, vasculogenesis and repair, 8/1/2006-5/31/2011.

Pending
NIH R21, Regulation of neuronal function by intracellular FGFs
NIH grant RO1 DC02236, Genes involved in the development of vestibular otoconia, renewal

Publications (Peer reviewed)

1. Renosto, F., Ornitz, D. M., Peterson, D., and Segel, I. H. (1981), Nitrate reductase from *Penicillium chrysogenum*: purification and kinetic mechanism, ***J. Biol. Chem.*** 256, 8616-8625

2. Ornitz, D. M., Palmiter, R. D., Hammer, R. E., Brinster, R. L., Swift, G. H., and MacDonald, R. J. (1985), Specific expression of an elastase human growth hormone fusion gene in pancreatic acinar cells of transgenic mice, ***Nature*** 313, 600-603

3. Ornitz, D. M., Palmiter, R. D., Messing, A., Pinkert, C. A., and Brinster, R. L. (1985), Elastase I promoter directs expression of human growth hormone and SV40 T antigen to pancreatic acinar cells in transgenic mice, ***Cold Spring Harb. Symp. Quant. Biol.*** 50, 399-409

4. MacDonald, R. J., Hammer, R. E., Swift, G. H., Ornitz, D. M., Davis, B. P., Palmiter, R. D., and Brinster, R. L. (1986), Tissue-specific expression of pancreatic genes in transgenic mice, ***Annals of the New York Academy of Sciences*** 478, 131-146

5. Hammer, R. E., Swift, G. H., Ornitz, D. M., Quaife, C. J., Palmiter, R. D., Brinster, R. L., and MacDonald, R. J. (1987), The elastase I regulatory element is an enhancer that directs correct cell-specificity and developmental onset of expression in transgenic mice, ***Mol. Cell. Biol.*** 7, 2956-2967

6. Ornitz, D. M., Hammer, R. E., Messing, A., Palmiter, R. D., and Brinster, R. L. (1987), Pancreatic neoplasia induced by SV40 T antigen expression in acinar cells of transgenic mice, ***Science*** 238, 188-193

7. Ornitz, D. M., Hammer, R. E., Palmiter, R. D., and Brinster, R. L. (1987), Promoter and enhancer elements from the rat elastase I gene function independently of other inducible and constitutive regulatory elements, ***Mol. Cell. Biol.*** 7, 3466-3472

8. Pinkert, C. A., Ornitz, D. M., Brinster, R. L., and Palmiter, R. D. (1987), An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice, ***Genes Dev.*** 1, 268-276

9. Quaife, C. J., Pinkert, C. A., Ornitz, D. M., Palmiter, R. D., and Brinster, R. L. (1987), Pancreatic Neoplasia Induced by Ras Expression in Acinar Cells of Transgenic Mice, ***Cell*** 48, 1023-1034

10. Ornitz, D. M., Moreadith, R. W., and Leder, P. (1991), Binary system for regulating transgene expression in mice: Targeting int-2 gene expression with yeast GAL4/UAS control elements, ***Proc. Natl. Acad. Sci. USA*** 88, 698-702

11. Yayon, A., Klagsbrun, M., Esko, J. D., Leder, P., and Ornitz, D. M. (1991), Cell surface, heparin-like molecules are required for binding of basic fibroblast growth factor to its high affinity receptor, ***Cell*** 64, 841-848

12. Benvenisty, N., Ornitz, D. M., Bennett, G. L., Sahagan, B. G., Kuo, A., Cardiff, R., and Leder, P. (1992), Brain tumors and lymphomas in transgenic mice that carry HTLV-I LTR/*c-myc* and Ig/*tax* genes., ***Oncogene.*** 7, 2399-2405

13. Ornitz, D. M., Cardiff, R. D., Kuo, A., and Leder, P. (1992), *Int-2*, an autocrine and/or ultra-short-range effector in transgenic mammary tissue transplants, ***J. Natl. Canc. Inst.*** 84, 887-892

14. Ornitz, D. M., and Leder, P. (1992), Ligand specificity and heparin dependence of fibroblast growth factor receptors 1 and 3, ***J. Biol. Chem.*** 267, 16305-16311

15. Ornitz, D. M., Yayon, A., Flanagan, J. G., Svahn, C. M., Levi, E., and Leder, P. (1992), Heparin is required for cell-free binding of basic fibroblast growth factor to a soluble receptor and for mitogenesis in whole cells, ***Mol. Cell. Biol.*** 12, 240-247

16. Peters, K., Ornitz, D. M., Werner, S., and Williams, L. (1993), Unique expression pattern of the FGF receptor 3 gene during mouse organogenesis, ***Dev. Biol.*** 155, 423-430

17. Tutrone, R. F., Jr., Ball, R. A., Ornitz, D. M., Leder, P., and Richie, J. P. (1993), Benign prostatic hyperplasia in a transgenic mouse: a new hormonally sensitive investigatory model, ***J Urol*** 149, 633-639.

18. Chellaiah, A. T., McEwen, D. G., Werner, S., Xu, J., and Ornitz, D. M. (1994), Fibroblast growth factor receptor (FGFR) 3. Alternative splicing in immunoglobulin-like domain III creates a receptor highly specific for acidic FGF/FGF-1, ***J. Biol. Chem.*** 269, 11620-11627

19. Deng, C. X., Wynshaw-Boris, A., Shen, M. M., Daugherty, C., Ornitz, D. M., and Leder, P. (1994), Murine FGFR-1 is required for early postimplantation growth and axial organization, ***Genes Dev.*** 8, 3045-3057

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23. Mathieu, M., Chatelain, E., Ornitz, D., Bresnick, J., Mason, I., Kiefer, P., and Dickson, C. (1995), Receptor binding and mitogenic properties of mouse fibroblast growth factor 3 (FGF3); modulation of response by heparin., ***J. Biol. Chem.*** 270, 24197-24203

24. Ornitz, D. M., Herr, A. B., Nilsson, M., Westman, J., Svahn, C.-M., and Waksman, G. (1995), FGF binding and FGF receptor activation by synthetic heparan-derived Di- and Trisaccharides, ***Science*** 268, 432-436

25. Westman, J., Nilsson, M., Ornitz, D. M., and Svahn, C.-M. (1995), Synthesis and fibroblast growth factor binding of oligosaccharides related to heparin and heparan sulphate, ***J. Carbohydrate Chem.*** 14, 95-113

26. Colvin, J. S., Bohne, B. A., Harding, G. W., McEwen, D. G., and Ornitz, D. M. (1996), Skeletal overgrowth and deafness in mice lacking fibroblast growth factor receptor 3, ***Nat. Genet.*** 12, 390-397

27. Lin, H. Y., Xu, J. S., Ornitz, D. M., Halegoua, S., and Hayman, M. J. (1996), The fibroblast growth factor receptor-1 is necessary for the induction of neurite outgrowth in PC12 cells by aFGF, ***J Neuroscience*** 16, 4579-4587

28. Naski, M. C., Wang, Q., Xu, J., and Ornitz, D. M. (1996), Graded activation of fibroblast growth factor receptor 3 by mutations causing achondroplasia and thanatophoric dysplasia., ***Nat. Genet.*** 13, 233-237

29. Ornitz, D. M., Xu, J., Colvin, J. S., McEwen, D. G., MacArthur, C. A., Coulier, F., Gao, G., and Goldfarb, M. (1996), Receptor specificity of the fibroblast growth factor family, ***J. Biol. Chem.*** 271, 15292-15297

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33. Herr, A. B., Ornitz, D. M., Sasisekharan, R., Venkataraman, G., and Waksman, G. (1997), Heparin-induced self-association of fibroblast growth factor-2. Evidence for two oligomerization processes, ***J Biol Chem*** 272, 16382-16389

34. McEwen, D. G., and Ornitz, D. M. (1997), Determination of fibroblast growth factor receptor expression in mouse, rat and human samples using a single primer pair, ***Biotechniques*** 22, 1068-1070

35. Miao, H.-Q., Ornitz, D. M., Aingorn, E., Ben-Sasson, S. A., and Vlodavsky, I. (1997), Modulation of fibroblast growth factor-2 receptor binding, dimerization, signaling, and angiogenic activity by a synthetic heparin-mimicking polyanionic compound., ***J. Clin. Invest.*** 99, 1565-1575

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38. Greene, J. M., Li, L. Y., Yourey, P. A., Gruber, J., Carter, K. C., Shell, B. K., Dillon, P. A., Florence, C., Duan, D. R., Blunt, A., Ornitz, D. M., Ruben, S. M., and Alderson, R. F. (1998), Identification and characterization of a novel member of the fibroblast growth factor family, ***Eur. J. Neurosci.*** 10, 1911-1925

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40. Lin, H.-Y., Xu, J., Ischenko, I., Ornitz, D. M., Halegoua, S., and Hayman, M. J. (1998), Identification of the cytoplasmic regions of fibroblast growth factor (FGF) receptor 1 which play important roles in the induction of neurite outgrowth in PC12 cells by FGF-1, ***Mol. Cell. Biol.*** 18, 3762-3770

41. McEwen, D. G., and Ornitz, D. M. (1998), Regulation of the fibroblast growth factor receptor 3 promoter and intron I enhancer by Sp1 family transcription factors, ***J. Biol. Chem.*** 273, 5349-5357

42. Naski, M. C., Colvin, J. S., Coffin, J. D., and Ornitz, D. M. (1998), Repression of hedgehog signaling and BMP4 expression in growth plate cartilage by fibroblast growth factor receptor 3, ***Development*** 125, 4977-4988

43. Ornitz, D. M., Bohne, B. A., Thalmann, I., Harding, G. W., and Thalmann, R. (1998), Otoconial agenesis in *tilted* mutant mice, ***Hearing Res.*** 122, 60-70

44. Wang, Y., Kowalski, P. E., Thalmann, I., Ornitz, D. M., Mager, D. L., and Thalmann, R. (1998), Otoconin-90, the mammalian otoconial matrix protein contains two domains of homology to secretory phospholipase A2, ***Proc. Natl. Acad. Sci., USA*** 95, 15345-15350

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46. Chellaiah, A., Yuan, W., Chellaiah, M., and Ornitz, D. M. (1999), Mapping ligand binding domains in chimeric fibroblast growth factor receptor molecules. Multiple regions determine ligand binding specificity, ***J. Biol. Chem.*** 274, 34785-34794

47. Colvin, J. S., Feldman, B., Nadeau, J. H., Goldfarb, M., and Ornitz, D. M. (1999), Genomic organization and embryonic expression of the mouse fibroblast growth factor 9 gene, ***Dev. Dyn.*** 216, 72-88

48. Li, H. S., Chen, J. H., Wu, W., Fagaly, T., Zhou, L. J., Yuan, W. L., Dupuis, S., Jiang, Z. H., Nash, W., Gick, C., Ornitz, D. M., Wu, J. Y., and Rao, Y. (1999), Vertebrate slit, a secreted ligand for the transmembrane protein roundabout, is a repellent for olfactory bulb axons, ***Cell*** 96, 807-818

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56. Wang, Q., McEwen, D. G., and Ornitz, D. M. (2000), Subcellular and developmental expression of alternatively spliced forms of fibroblast growth factor 14, ***Mech. Dev.*** 90, 283-287

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84. Umemori, H., Linhoff, M. W., Ornitz, D. M., and Sanes, J. R. (2004), FGF22 and Its Close Relatives Are Presynaptic Organizing Molecules in the Mammalian Brain, ***Cell*** 118, 257-270

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95. Zhang, X., Stappenbeck, T. S., White, A. C., Lavine, K. J., Gordon, J. I., and Ornitz, D. M. (2006). Reciprocal epithelial-mesenchymal FGF signaling is required for cecal development. ***Development*** *133*, 173-180.

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97. White, A. C., Xu, J., Yin, Y., Smith, C., Schmid, G., and Ornitz, D. M. (2006). FGF9 and SHH signaling coordinate lung growth and development through regulation of distinct mesenchymal domains. ***Development*** *133*, 1507-1517

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102. Park, C., Lavine, K., Mishina, Y., Deng, C. X., Ornitz, D. M., and Choi, K., (2006). Bone morphogenetic protein receptor 1A signaling is dispensable for hematopoietic development but essential for vessel and atrioventricular endocardial cushion formation. ***Development.***

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104. Gutin, G, Fernandes, M, Palazzolo, L, Paek, H, Yu, K, Ornitz, DM, McConnell, S. K., and Hebert, J. M., (2006). FGF signalling generates ventral telencephalic cells independently of SHH. ***Development*** *133*, 2937-2946.

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106. Wozniak, DF, Xiao, M, Xu, ., Yamada, KA, and Ornitz, DM, (2007). Impaired Spatial Learning and Defective Theta Burst Induced LTP in Mice Lacking Fibroblast Growth Factor 14. ***Neurobiol Dis,*** 26, 14-26.

107. Xiao, M, Xu, L, Laezza, F, Yamada, K, Feng, S, and Ornitz, DM, (2007). Impaired hippocampal synaptic transmission and plasticity in mice lacking fibroblast growth factor 14. ***Mol Cell Neurosci***, 34, 366-377.

108. Lin Y, Liu G, Zhang Y, Hu YP, Yu K, Lin C, McKeehan K, Xuan JW, Ornitz DM, Shen MM, Greenberg N, McKeehan WL, Wang F. (2007). Fibroblast growth factor receptor 2 tyrosine kinase is required for prostatic morphogenesis and the acquisition of strict androgen dependency for adult tissue homeostasis. ***Development*** 134:723-734.

109. Liu, Z, Lavine, KJ., Hung, IH., and Ornitz, DM, (2007) FGF18 is required for early chondrocyte proliferation, hypertrophy and vascular invasion of the growth plate, ***Dev Biol*** 302(1), 80-91.

110. Smith, SM, West, LA., Govindraj, P, Zhang, X, Ornitz, DM., and Hassell, JR, (2007). Heparan and chondroitin sulfate on growth plate perlecan mediate binding and delivery of FGF-2 to FGF receptors. ***Matrix Biol*** *26*, 175-184.

111. Hung, IH, Yu, K, Lavine, KJ, Ornitz DM, (2007). FGF9 regulates early hypertrophic chondrocyte differentiation and skeletal vascularization in the developing stylopod. ***Dev Biol,*** in press.

112. Hughes, I., Saito, M., Schlessinger, P. H., and Ornitz, D. M. (2007) Otopetrin1: a novel purinergic nucleotide-gated regulator of intracellular calcium, ***Proc Natl Acad Sci U S A,*** in revision.

113.

Book chapters and reviews:

1. Ornitz, D. M., Skoda, R., Moreadith, R. W. and Leder, P. (1992). Regulating Gene expression in mammalian cell culture and transgenic mice with yeast GAL4/UAS control elements. NATO ASI series. Oncogene and transgenic correlates of cancer risk assessments. Zervos, C.,
2. Ornitz, D. M. and Waksman, G. (1997). Fibroblast growth factor receptors. Growth factors and wound healing: Basic science and potential clinical applications. New York, Springer-Verlag. Ziegler, T. R., Pierce, G. F. and Herndon, D. N., 151-174.
3. Naski, M. C. and Ornitz, D. M. (1998). FGF signaling in skeletal development. Front. Biosci. 3, D781-794.
4. Thalmann, R., Echols, R., Wang, Y., Thalmann, I. and Ornitz, D. M. (1999). Unresolved issues of biology and pathology of otoconia. in Equilibrium in research and equilibriometry and modern treatment. Amsterdam, Elsevier Science. Clausen, C.-F. 113-119
5. Ornitz, D. M. (2000). FGFs, heparan sulfate and FGFRs: complex interactions essential for development. Bioessays 22, 108-112
6. Ornitz, D. M. (2000). Fibroblast growth factors, chondrogenesis and related clinical disorders. Skeletal growth factors. Philadelphia, Lippincott Williams & Wilkins. Canalis, E., 197-209.
7. Ornitz, D. M. and Itoh, N. (2001). Fibroblast growth factors. Genome Biology, 3005.1-3005.12.
8. Ornitz, D. M. (2001). Regulation of chondrocyte growth and differentiation by fibroblast growth factor receptor 3. In The molecular basis of skeletogenesis, G. Cardew, and J. A. Goode, eds. (Chichester, John Wiley and Sons, Ltd.), pp. 63-80.
9. Yu, K., and Ornitz, D. M. (2001). Uncoupling FGF receptor 2 activation and ligand binding specificity: Multiple paths to Apert syndrome-like phenotypes., Proc. Natl. Acad. Sci., U S A, 98, 3641-3643.
10. Ornitz, D. M. (2001). Regulation of chondrocyte growth and differentiation by fibroblast growth factor receptor 3. Novartis Found Symp 232, 63-76; discussion 76-80, 272-82.
11. Ornitz, D.M. and Marie, P. J. (2002). FGF signaling pathways in endochondral and intramembranous bone development and human genetic disease. Genes Dev., 16, 1446-1465
12. Ornitz, D. M. (2003) Evolution of Fibroblast Growth Factors, in Encyclopedia of the Human Genome, pp. in press, Nature Publishing Group, New York
13. Itoh, N., and Ornitz, D. M. (2004), Evolution of the *Fgf* and *Fgfr* gene families, Trends Genet. 20, 563-569.

14. Ornitz, D. M. (2005). FGF signaling in the developing endochondral skeleton. Cytokine Growth Factor Rev *16*, 205-213.

15. Ornitz, D. M., and Sannes, P. (2005) FIBROBLAST GROWTH FACTORS. In. Encyclopedia of Respiratory Medicine, Elsevier Ltd.

16. Hughes, I., Thalmann, I., Thalmann, R., and Ornitz, D. M. (2006),. Mixing model systems: Using zebrafish and mouse inner ear mutants and other organ systems to unravel the mystery of otoconial development. Brain Res.

17. Lavine, KJ, Ornitz, DM, (2007), Rebuilding the coronary vasculature: hedgehog as a new candidate for pharmacologic revascularization. Trends Cardiovasc Med 17, 77-83.

18.

Publications in preparation or submitted

Hedgehog signaling to distinct cell types differentially regulates coronary artery and vein development

FGF signaling regulates mesenchymal differentiation and skeletal patterning along the limb bud proximodistal axis

FGF-Wnt signaling interactions regulate lung mesoderm development.

Invited Seminars

Washington University, Dept. of Genetics, October 1992; Dupont/Meck, October, 1992; New York University, Dept. of Cell Biology, April, 1994; University of Pennsylvania, Research Center in Oral Biology, April 1994; Harvard Medical School, Dept. of Genetics, June 1994; Millenium Pharmaceuticals, June 1994; Washington University, Dept. of Hematology, October 1994; Prizm Pharmaceuticals, January 1995; Jewish Hospital, St. Louis, Dept. of Medicine, June 1995; Mount Sinai Medical Center, Brookdale Center for Molecular Biology, October 1995; Purdue University, Biochemistry and Molecular Biology Program, October 1995; University of Washington, Biochemistry, February 1996; Children's Hospital, St. Louis, Pediatric Grand Rounds, June 1996; University of Connecticut Medical School, October, 1996; Bayer Pharmaceuticals Inc., October, 1996; Human Genome Science Inc., October, 1996; Hartman Institute, University of Helsinki, Molecular/Cancer Biology Laboratory, November, 1996; Ludwig Institute for Cancer Research, Stockholm Branch, Karolinska Institute, November, 1996; McGill University Medical School, March, 1997; Lady Davis Institute for Medical Research, Montreal, March, 1997; Washington University, Dept. of Neurology, April, 1997; Sigma Chemical Co., St. Louis, March 1997; Schriners Hospital, Portland, Oregon, December, 1997; Dept. of Biol. Sciences and Technology, Tokushima University, Tokushima City, and Niigata University School of Dentistry, Niigata, Japan, February 1998; University of Colorado, Boulder, April 1998; St. Louis University, Dept. of Molecular Microbiology and Immunology, February, 1999; UC Irvine, Dept. of Developmental Biology, April, 1999; SUNY, Stony Brook, Dept. of Molecular Genetics and Microbiology, April, 1999; University of Wisconsin, Madison, Dept. of Anatomy, May, 1999; Swiss Federal Institute of Technology, Zurich, October 1999; University of Washington, Dept. of Pharmacology, October, 1999; Zymogenetics Inc., Seattle, October, 1999; King's College London, Guy's Hospital campus, November, 1999;

MD Anderson Cancer Center, Houston, TX, January, 2000; NYU Medical School, NY, February, 2000; Mount Sinai Medical School, NY, February 2000; Saint Louis University, Dept. of Biology, October, 2000; Vision Science Training Grant, University of Washington, Seattle, January, 2001; Zymogenetics Inc. January, 2001; Pharmacia Inc. Kalamazoo, June, 2001;

ImClone Inc., NYC, October, 2001; UMDNJ, Newark, October, 2001; University of Leuven Medical School, Leuven, Belgium, November, 2001; Institute Curie, Paris, France, November, 2001; Max Planck Institute for Genetics, Berlin, Germany, November, 2001; Renal Division, Washington University, November, 2001; Stowers Institute for Medical Research, February, 2002; University of Chicago, Dept. of Molecular Genetics and Cell biology, March 2002; Cardiology Division, Washington University, May 2002; Salk Institute, May, 2002; Okayama University Medical School, June, 2002; Kyoto University, July, 2002; Siteman Cancer Center Basic Science Seminar Series, September, 2002; University of Oulu, October, 2002; University of Helsinki, October, 2002; Dept. Cell Biology, Washington University, November, 2002; Cell Signaling, Duke University Medical School, November, 2002; Lineberger Comprehensive Cancer Center, UNC, February, 2003; Neuroscience Center, UNC, February, 2003; Division of Cardiology, UCSD, April, 2003; Bone conference, Washington University, April, 2003; Chiba University, Japan, June, 2003; NYU Medical School, Dept. of Pharmacology, November, 2003; Shriners Hospital, Oregon health Science University, December, 2003; National Cancer Institute, Frederick, MD, February, 2004; Children's Hospital, Boston, Dept. Orthopedic Surgery, October, 2004; UT Southwestern, Dallas, Molecular Biology seminar series, November, 2004; Oxford University, Oxford, UK, December, 2004; University of Nebraska Medical School, Omaha, January, 2005; University of Southern California, February, 2005; Endocrine Grand Rounds, Massachusetts General Hospital, Boston, March, 2005; Renal division, Washington University, April, 2005; ETH Zurich, May, 2005; Pulmonary Medicine, Washington University, November, 2005; NIDCD council, January, 2006; NHGRI, January, 2006; Molecular Biology & Pharmacology, Washington University, April, 2006; University of Cincinnati, April, 2006; Genentech Inc., April, 2006; Enobia Pharmaceuticals, Montreal, April, 2006; Medical College of Georgia, May, 2006; Eli Lilly, August, 2006; University of Iowa, Dec. 2006; Radiation Oncology, Washington University, Dec. 2006; University of Utah, February, 2007; Baylor College of Medicine, April, 2007;

Speaker at Conferences

International Genetic workshop on Crouzon and other Craniofacial Disorders, Philadelphia, March 1995; Gordon Conference on Collagen, July 1995; International Symposium on Growth Factors and Wound Healing: Basic Sciences and Clinical Applications (Serono Symposium USA), Boston, September 1995; Keystone Symposium on Signal Transduction through Tyrosine Kinases, March 1996; Gordon Conference on Peptide Growth Factors, August 1996; American Society for Bone and Mineral Research, Plenary speaker, Seattle, September, 1996; 2nd GAAS meeting on Molecular Medicine: The Role of Growth Factors in Human Disease, Munich, November 1996; Gordon Conference on Bone and Teeth, July 1997; Gene function *in vivo*: The Impact of Gene Targeting, Research Workshop of the Israel Science Foundation, September, 1997; Molecular Signaling in Development, Cell Differentiation and Proliferation, Tokyo Medical and Dental University, Tokyo, February 1998; Alternative Biology of Fibroblast Growth Factors, Edinburgh, Scotland, March 1998; Gordon conference on Bioengineering and Orthopedic Science, July, 1998; The Role of Cytokines in Human disease II, Kloster Seeon, Germany, August, 1998; NIDCD workshop, Role of Transgenic and Knockout Studies in Understanding Sensory-Motor Performance in Altered Gravitational Environments, Bethesda, MD, June 1999; Gordon Conference, Development, June, 1999; German Genetic Society, Developmental Genetics, Munich, October 1999; Novartis Foundation, The Molecular Basis of Skeletogenesis, London, November, 1999; EMBO Workshop of FGF and their Receptors: Structure to Function, Ein Gedi, Israel, December 1999;
American Society of Human Genetics, Philadelphia, October, 2000; Biology and Pathology of the Extracellular Matrix, Plenary speaker, St. Louis, October, 2000; Keystone Symposium on Integration of Signaling Pathways in Development, January, 2001; American Heart Association, May, 2001; Gordon conference, Tissue repair and wound healing, June, 2001; Gordon

conference, Bone and Teeth, August, 2001; MD Anderson Cancer center symposium, October, 2001; International Titisee Conference, Growth Factors in Development, Repair and Disease, Titisee, Germany, March, 2002; American Society for Endocrinology, San Francisco, June, 2002; Japanese Endocrine Society, Osaka, June, 2002; Mouse Molecular Genetics, CSHL, August, 2002; Skeletal Development, Lucca, Italy, October, 2002; Arizona Cancer Center meeting on Multiple Hereditary Exostoses, Tuson, AZ, October, 2002; Birth defects meeting, NIH, December, 2002; Biology and Pathology of Cartilage, Gordon conference, Ventura, CA, March, 2003; Experimental Biology, ASBMB, San Diego, April, 2003; American Society for Neuro Chemistry, Newport Beach, May, 2003; International Society Bone and Mineral Research/Japan Society Bone and Mineral Research, Osaka, June, 2003; Ninth Canadian Connective tissue conference, Montreal, July, 2003; FASEB meeting Tucson, Growth factor tyrosine kinases, August, 2003; ASBMR, Minneapolis, September, 2003; International meeting on Fibroblast Growth Factors, Kobe, Japan, October, 2003; Gordon conference on Craniofacial Morphogenesis and Tissue Regeneration, January, 2004; Keystone symposia, Signaling in vertebrate organogenesis, February, 2004; Experimental Biology, AAA, Washington DC, April, 2004; ARVO (Association for Research in Vision and Ophthalmology), April, 2004; Leder lab reunion symposium, June, 2004; Mouse Molecular Genetics, CSHL, September, 2004; Clive Dickson symposium, London, December, 2004; Southern Illinois University 11th Annual Molecular & Cellular Biology symposium, Keynote speaker, April, 2005; Hinterzartener Kreis for Cancer Research, Cadenabbia, Italy, May, 2005; GRC, Cartilage growth and repair, Italy, June, 2005; ASBMR, September 2005, Nashville; MHE coalition meeting, November 2005, Houston; Craniofacial development, GRC, Ventura, January, 2006; FGF GRC, March 2006, Ventura; FASEB-Experimental Biology, San Francisco, April, 2006; Growth Plate Workshop, June 2006, Portland; Endocrine Society, June, 2006, Boston; Mouse Molecular Genetics, September, 2006; Esteve Symposium, October, 2006, Spain; American Acadamy Othopoedic Surgery, October, 2006, Toronto; Spring Brain Conference, Sedona, AZ, March, 2007; Palmiter symposium-RP65, Seattle, April, 2007;

Future conferences

Intracellular Transport and Signal Transduction in Cancer Biomedicine, Norway, May 2007
CSHL mouse course, June, 2007
FGF signaling Gordaon Conference, Italy, March 2008

Teaching

Nucleic Acids, Discussion Section Leader, Fall 1993, Fall 1994
Molecular Cell Biology, Discussion Section Leader (10 hr), Fall 1995-1998
Advanced Genetics, Lecture, (2 hr) Spring 1995, (3 hr) Spring 1996-2007
Molecular Biology and Pharmacology Journal Club, organizer, 1993/1994
Molecular and Developmental Biology Journal Club, organizer, 1995-2000
Central questions in Cell Biology, Lecture (4 hr), Fall 1995
Molekoolz, the course, Lecture (1.5 hr), winter 1996, winter 1997, winter 2000.
Molecular Neurobiology, Lecture (1 hr), winter 1997
Bio5011, Ethics in Research Science, Section Leader, winter 1997
Signaling and Human Biology, Section organizer (8 hr), lecture (1 hr.) discussion (2 hr.), Spring 2002, 2003
Developmental Biology and Disease, Medical student elective, 3 hr, Spring 2006, 2007

Student Mentoring

Current Ph.D. students in lab:
Sung-Ho Huh
Euysoo Kim
Monica Vega-Hernandez
Marie Kozel

Past students in lab:
Huacheng Ying, MS, July 1996, Thesis title: Positional cloning of the tilted locus,
Don McEwen, Ph.D., January, 1998, Thesis title: FGFR3 gene regulation, Current, Postdoctoral fellow with Mark Peifer, University of North Carolina, Assistant professor, University of Texas, Austin, 2006-
Jennifer Colvin, M.D. Ph.D. March, 1999, Thesis title: Developmental role of FGFR3 and FGF9, MD, 2001, Current, Fellow in Child Psychiatry, Duke University Medical School.
Jingsong Xu, Ph.D. September, 1999, Thesis title: Midbrain-hindbrain development, , Postdoctoral fellow with Steve Shapiro, Harvard Medical School, Current, Research Associate, Harvard Medical School.
Qing Wang, Ph.D. February, 2001, Studies of mice lacking FGF14, Current position, patent division, Monsanto Inc, St. Louis, MO.
Wenlin Yuan, Ph.D., June, 2002, biology of slit genes. Current, postdoctoral fellow with Timothy Ley, Washington University Medical School
Kai Yu, Ph.D., July, 2002, FGF receptor 2 function in bone growth and development. Current, postdoctoral fellow in my laboratory.
Zhonghao Liu, Ph.D. August, 2003, FGF18 signaling in bone growth and vasculogenesis. Current, postdoctoral fellow with Alan Permutt, Washington University Medical School.
JL Lou, Ph.D. January, 2005, The Modulation of Voltage-Gated Sodium Channels and Neuronal Excitability by FGF14. Current, Resident in Internal Medicine, Duke University.
Andrew White, Ph.D. March 2005, Fibroblast Growth Factor 9 Regulates Mesenchymal Gene Expression and Regional Proliferation to Coordinate Developing Lung Shape and Size with Epithelial Morphogenesis and Blood Vessel Vasculogenesis. Current, postdoctoral fellow, Ornitz lab
Inna Hughes, Ph.D. mechanism of Otopetrin 1 regulation of cellular calcium. December, 2005, Current, MSTP student.
Kory Lavine, Ph.D. May, 2006, Heart vascular development, MSTP student
Chad Perlyn, M.D., Ph.D. (Oxford University Ph.D. June 2006), Fellow in plastic surgery, WUSM.

Current postdoctoral fellows:
Maolei Xiao, Ph.D.
Kai Yu, Ph.D.
Hidemi Kanazawa, M.D., Ph.D.
Yongjun Yin, Ph.D.
Andrew White, Ph.D.
Fernanda Laezza, M.D, Ph.D.

Past postdoctoral fellows:
Becky Green, M.D., Ph.D. 1999-present instructor, Pediatric Endocrinology, St. Louis Children's Hospital
Mike Naski, M.D., Ph.D. 1997-present, Assistant Professor, UT San Antonio
Al Blunt, M.D. (Covance Inc.)

Yunxia Wang, Ph.D. 1998-present, Research Assistant Professor, U. Nebraska-Medical Center
Arasu Chellaiah, Ph.D. (self employed)
Sylvia Santos-Ocampo, M.D. 1995-present, Clinician
Luke Bruns, M.D. 1999-present, Clinician
Belen Hurle, Ph.D., 2002-present, Research Associate, NIH
Zhonghao Liu, Ph.D., 2004-present, postdoctoral fellow with Alan Permut
Irene Hung, M.D. 2002-2005, Genetics fellow, Department of Pediatrics., University of Utah
Anne Jacob, Ph.D. Research Associate, University of Oslo,
Xiuqin Zhang, Ph.D., Faculty, Beijing University.

Committees

Molecular and Cellular Biology Steering Committee, 1992-present
Transgenic/Barrier Sub-Committee, 1995-present
Washington University Cancer Center, Basic Science Sub-Committee, 1995-present
Developmental Biology Steering Committee, 1997-present
Mouse behavior core steering committee, 1999-present
Member, Washington University Advisory Board to Sigma -Aldrich Research, Molecular Biology Product Initiatives, 1997 – 2001.
Member, Scientific Advisory Board, Sigma-Aldrich, 2002-present.
Committee for Research Integrity, Ad hoc member, May 2002. July 2005
Executive Faculty, Washington University 10/2004-present.

Directorships

Washington University Cancer Center Developmental Biology group. June 1997-present
Program in Developmental Biology, Division of Biology and Biomedical Science. May 1998-May 2001.

Conference chair

Gordon Research Conference on Fibroblast Growth Factors in Development and Disease. March, 2006.

Reviewing

Cell; Nature; Genes & Development; Science; Neuron; Development; Nature Genetics; Nature Medicine; Developmental Biology; Developmental Dynamics; Mechanisms of Development; J. Biological Chemistry; Biochemistry; J. Cell Biology; J. Cell Physiology; Blood; Nucleic Acid Research; J. Neuroscience; J. Cellular Biochemistry; Transgenic Research; PNAS; Molec. Endocrinology; Exp. Eye Research; Cancer Communications; Endocrine Review; Oncogene; J. Bone Mineral Research; Bone; Human Molecular Genetics; J. Clinical Investigation; others

Study sections

Ad hoc reviewer for NIH-CBY-1, October 1998
Ad hoc reviewer for NIH-CDF-5, June 1999
Beckman Young Investigator Program, November, 1999, November 2000, November 2001
Special emphasis panel for NIH HL-99-024, Genomic applications for Heart, Lung and Blood Research, June 2000
Special emphasis panel for NIH DC-01-00, Studies of sensory-motor functions responsive to gravity in genetically altered model systems, April, 2001.
Special emphasis panel for NIH DA-01-011, Insertional mutagenesis in the mouse, July, 2001
NIDCD Special emphasis panel for NIH PAR-01-103, November, 2001
NIDCD, ZDC1 SRB-A, ad hoc member, November, 2002

NCI, Cancer center site visit, Columbia University, January, 2003
Ad hoc reviewer, NIH-BIO, Biochemistry Study Section, March, 2003
Ad hoc reviewer, Pathobiochemistry study section, February, 2004
NCI, internal review, Fredrick MD, April, 2004
ZRG1 MDCN-A study section, July, 2004
ZRG1 CDD- Cardiovascular Differentiation and Development study section, October 2004
Dev2, member, 2005-2009

Societies

American Association for the Advancement of Science (AAAS)
Society for Developmental Biology (SDB)
Society for Neuroscience (SfN)

Editorial board

Developmental Dynamics

Research Abstract

Fibroblast growth factors (FGFs) are essential molecules for mammalian development. Members of the FGF family regulate cell proliferation, migration and differentiation. Engineered mutations in the genes encoding several FGFs and FGF receptors (FGFRs) result in developmental defects and/or embryonic lethality. Additionally, gain of function point mutations in the genes encoding FGFRs 1, 2 and 3 results in hereditary craniofacial and skeletal dysplasias in humans.

We have recently discovered that a subfamily of FGFs (FHFs) acts intracellularly in neurons and is important for neuronal signal transduction. Disruption of the intracellular signaling molecule, FGF14/FHF4 results in an anatomically normal mouse with severe neurobehavioral phenotypes including ataxia, paroxysmal dystonia and cognitive impairment. We are interested in the mechanism by which FGF14 regulates neuronal excitability in the cerebellum and hippocampus. We are also studying how FGF14/FHF4 regulates presynaptic function and short and long-term potentiation.

We are also studying the more classical FGFs and FGF receptors in mouse embryogenesis. Using knockout and conditional knockout technology we have constructed FGF and FGF receptor mutants with defects in skeletal, lung, heart and CNS development. These mutant mice are being studied as developmental model systems for branching morphogenesis, vasculogenesis and skeletal and neuroepithelial patterning and growth. These mice are also being used as material for microarray profiling studies to identify interacting gene families.

Future directions

My laboratory will continue to study the function of FGF signaling in four main areas:

1. Central nervous system development and neurophysiology
2. Lung development
3. Heart development
4. Skeletal development

Goals will be to identify novel interacting signaling molecules and novel downstream effectors of FGF signaling. In addition to focusing on existing FGF ligand knockout mice we have now made a functional conditional allele for FGF receptor 2. We will inactivate FGF receptor 2 using tissue-specific and temporal-specific expression of Cre recombinase. Novel techniques that are being applied include microarray analysis of knockout mice, organ culture and bead implantation on tissue derived from knockout mice.

We will continue to work on understanding the molecular and developmental function of the *Otopetrin* gene. A mutation in *Otopetrin* is responsible for the tilted mouse phenotype.

Otopetrin was positionally cloned in my laboratory. Collaborative experiments are planned to examine Otopetrin expression and function in the vestibular system at different gravitational intensities.